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Award Number: DAMD17-94-J-4327

TITLE: Breast cancer screening by physical examination: randomized trial in the Philippines

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REPORT DATE: October 2002

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

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REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 074-0188

1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	October 2002	Annual (30 Sep 2001 -29 Sep 2002)

4. TITLE AND SUBTITLE

Breast cancer screening by physical examination: randomized trial in the Philippines

5. FUNDING NUMBER
DAMD17-94-J-4327

6. AUTHOR(S)
D. M. Parkin, M.D.

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

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8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSORING / MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

12b. DISTRIBUTION CODE

13. ABSTRACT *(Maximum 200 Words)*

Completed activities.

- Breast cancer incidence by end of 1999 in all project cohorts.
- record linkage between files of incident cases and master files of the intervention cohort;
- continuing identification and registration of all cases of malignant cancer in the resident population;
- Re-interview of 123 cases and 978 matched controls selected from the screened cohort.
- Data analysis and reporting.

On-going

- Cancer registry follow-up procedures have been established and breast cancer cases are recorded regularly. Clinical details of stage at diagnosis are sought systematically for all cases.
- Data analysis and reporting.

14. SUBJECT TERMS
breast cancer, physical exam, data analysis

15. NUMBER OF PAGES
20

16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	Unlimited

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(4) INTRODUCTION

In the year 2000 breast cancer accounted for over 1 million new cases per year worldwide (Ferlay *et al.*, 2001), and it was the most common cancer in women. Incidence rates are still rising in many countries, particularly in low-risk countries (Parkin *et al.*, 2001). It seems that these trends are likely to continue, since the current pattern of later childbearing, decreasing fertility, and 'westernization' of diets will all be associated with increased risk.

At present, our knowledge of environmental risk factors does not permit formulation of any practical primary prevention programs. The introduction of adjuvant therapy with Tamoxifen has improved survival of older cases and a decline of mortality from breast cancer below age 50, observed in some high-risk countries, has also been attributed to adjuvant therapy (Nab *et al.*, 1994, Olivotto *et al.*, 1994). However, further improvements in surgical techniques, or in radiotherapy, are very unlikely to provide more than marginal changes in mortality rates.

A much greater decrease in deaths from breast cancer is achievable through screening programs which lead to detection of cancers which are smaller, at an earlier stage, and less malignant than those which surface clinically. An extensive and comprehensive review of the efficacy of different screening modalities for the breast has been published recently (IARC, 2002). The volume includes all relevant published studies as well as the newest data. It is the product of the collaboration of an international working group of experts who conclude the work with an evaluation of the degree of evidence for the efficacy of the screening procedures described. The working group agreed that there is sufficient evidence that mammography can reduce breast cancer mortality by 25% in women 50-69 years of age. It is also recognized that the performance of population screening programs by mammography may achieve that impact on mortality only by maintaining high participation rates, high sensitivity of the test, accurate diagnostic investigation of screen-positive women, and timely treatment of detected cases. Mammograpahy is an expensive technology that requires highly trained radiologists and radiographers. The cost per life-year saved, having to meet all the conditions described above, is therefore relatively high (Barnum and Greenberg, 1991), and clearly an inappropriate use of health care resources for many countries (WHO, 1984).

The alternative screening strategies which have been proposed are physical examination of the breasts (PE), and breast self-examination (BSE). The results of the only randomized trial of BSE ever conducted have been published this year (Thomas *et al.*, 2002). It is a large scale trial among 266,000 textile workers in Shanghai, China, conducted by researchers of the University of Washington. Biases such as low compliance with the intervention, failure of proper randomization or low proficiency in performing BSE could be confidently excluded (Thomas *et al.*, 1997). No significant reduction of breast cancer mortality in the intervention group has been detected after 10 years of follow-up and the distribution of stage at diagnosis in screen and control groups were very similar. Evidence was provided that this result was not attributable to biases or low statistical power. Nevertheless, the small size of the lesions diagnosed in the control subjects in this trial (47 % $\leq$2 cm diameter, 48% node negative) suggests a high level of health-awareness in the Shanghai population, and may give little scope for improvement in outcome through early detection by BSE.

At present PE has never been used as the sole modality of screening, so that its effectiveness is not known. Indirect evidence based on estimates of the accuracy of PE relative to mammography suggests that this type of

examination could reduce mortality rates by 2/3 to 3/4 of that achievable by mammography screening in women aged 50 or more. PE alone may be effective in younger women, among whom up to 25% cancers are missed by mammography; in addition, there is evidence that PE improves the performance of mammography. The working group who reviewed in 1979 the results of the Breast Cancer Detection Demonstration Project, the first large non-experimental evaluation of mammography, stated that high priority should be given to the evaluation of PE as a single screening modality (Nelson, 1997). The recommendation was not followed by action until the project described here, possibly because of the rapid spreading of mammography in most developed countries, which vitiated the feasibility of an unscreened control group.

The purpose of the present work was to establish 1) whether a program of mass screening by PE performed by trained paramedical personnel could be set up in a developing country as part of the routine activity of first level health services, and 2) whether and to what extent such a program could reduce mortality from breast cancer. The location is Metro Manila and Rizal Province of the Philippines. This population has a relatively high incidence of breast cancer, considerably above that of other Asian populations, and comparable to that in southern Europe.

(5) **BODY**

The study was a randomized controlled trial of the effect of annual physical examination (PE) of the breasts performed by trained nurses/midwives, in reducing mortality from breast cancer. The study area comprised the central, more urbanized municipalities of the National Capital Region (Districts I, II, III and IV), which includes 12 municipalities each having municipal health centers in the township area and barangay health stations in more rural areas. In 1990, the estimated size of the female population aged 35-64 was about 340,000. The units of randomization were health centers (HCs) within the selected municipalities of the Manila - Rizal area.

Women aged 35-64 years resident in the intervention HC areas were offered annual breast examinations, carried out by specialized midwives/nurses. At the first visit, these women were also instructed in the technique of breast self-examination (BSE) and provided with a leaflet in the local language explaining the purpose and methodology of BSE.

Women in the control area received no active intervention, but were exposed to the general health education campaigns carried out by municipal authorities and voluntary bodies.

The examiners were trained using a program already developed and tested in the Philippines, making use of breast silicon models. Training was repeated for selected groups of examiners with detection rates markedly above or below the mean. Women eligible for screening were invited to participate through a variety of mechanisms including home visits.

At the first visit women were interviewed to record demographic variables and risk factors for breast cancer. Instruction in BSE was given and PE performed. Demographic characteristics of women who refused PE were also recorded.

Women with detected abnormalities were referred for final diagnosis to special clinics, made available in 3 major hospitals staffed by project personnel. After one year of intervention, compliance with referral was only 21% and all remedies put in place to improve it (see below), did not significantly affect the proportion of positive women who reached a definitive diagnosis. The intervention was therefore discontinued after the completion of the first round and follow-up of the intervention and control cohorts has been undertaken.

The first follow-up phase (2 years after the intervention) was terminated in early 2002. In this report we present some early results of the outcome of the intervention, the cumulative incidence of breast cancer by December 1999 in the two groups, a comparison of stage at diagnosis in screen-detected and clinical cases, and the results of ancillary studies that exploit the information accumulated during the running of the project. In particular we present an analysis of risk factors for breast cancer in this population, based on data collected during the intervention. By the same data we estimated that 30% of all cases occurring in this population is attributable to low parity (less than 3 children or 1st pregnancy at age 21+ years). Trends towards lower fecundity rates account for only one third of the incidence. To complete this long-term project we propose a study of genetic determinants of the disease, which exploits the experience and data accumulated through the intervention project.

Results in chronological order.

Table 1 describes the content and size of the computerized files that have been created all along the conduction of the study. They are described in greater detail below and in previous reports.

A) Intervention

During 1995 a coordinating center was set up. Two hundred and two Health Centers were randomized to intervention and control arms. Hospital clinics for referral of positive women and mechanisms for documentation of results were established.

Personnel from the intervention HCs were recruited and trained. It soon became evident that the regular personnel of HCs could not reach the scheduled rate of 14,000 woman-examinations per month. Therefore, nurses were recruited to work full-time for the project (FTNs). In March 1996, the intervention reached a regular pace. The first round of the intervention was completed in December 1997. The results of the intervention after completion of the single round of examinations, are summarized in Table 1. Three-thousand four hundred and ninety two women were detected positive for a lump at first examination. Of these, 42.3% actively refused further investigation, 21.8% who did not report to the tumor clinics had moved away or died when visited at home and seventy-one cases (2%) are waiting for final diagnosis. Only 32% (1,108 women) completed the diagnostic process, of these 31 were malignant cancers detected. The outcome of the intervention is summarized in table 2.

Comparison of characteristics of compliers and refusers.

In the annual report of 1997 we presented an analysis of the characteristics of a sample of women who accepted PE and of those who refused it. The two groups do not differ by age, prevalence of smoking or compliance with screening for cervix cancer, the latter being an indicator of the general attitude towards preventive practices. In contrast with what is observed in western countries, refusers are of higher social class, as indicated by greater average income and significantly lower parity (table 3).

Interview of a sample of 999 women resident in the control area (years 1999-2000).

A sample of 2,000 names, stratified by age, was drawn from the file of the eligible population in the control HCs. Two interviewers were recruited and trained to trace and perform interviews according to the questionnaire used in the intervention phase. Interviewers were provided with many more suitable names to allow for the turn-over of the resident population (migrated or deceased). The target number was 1,000. The purpose of this sample survey was to estimate the actual proportion of the control cohort that was present in 1999, and to compare the characteristics of this cohort with those of the intervention group as a check on the randomization procedure. Thirty eight percent of the women in the original lists of resident population could not be traced. Nine-hundred and ninety nine interviews were completed. Women in the control areas, as assessed through the sample, were of similar age at interview and age at menarche compared to women in the intervention arm. Control women however, were of lower age at first birth, a higher proportion of them was parous and a significantly greater proportion declared to drink alcohol regularly.

Action taken to improve compliance with clinical investigation among women detected positive.

One thousand women who were positive for a lump at the initial visit but who had not subsequently turned up at a referral clinic were visited a second time to assess the motives for non-compliance. The survey indicates that the main reasons for non-compliance are inconvenience and cost. In order to induce greater motivation to seek medical attention, medical teams formed by a doctor and a nurse and equipped to perform needle biopsies, were sent to visit non-compliers at home in order to obtain a final diagnosis. This activity commenced in March 1997 (recruitment and training of doctors) and was completed by end of April 1998. The results of active clinical follow up are also presented in Table 2.

Second attempt to improve compliance of positive women with clinical follow-up.

Forty-three percent of the 3,472 women detected positive for a lump at 1st examination, refused biopsy and further clinical investigations. A second attempt to motivate these women towards diagnosis and treatment if required has been performed in year 2000. Seventy of the positive women, who complied with clinical examination by a doctors but refused biopsy were contacted by nurses and offered a second examination by a doctor. The visits took place in the Health Centers of the women's residence. Four malignant cancers were detected (detection rate is 6%); 17 resulted negative for a lump at palpation, 10 (14%) had fibrocystic disease; 19 needed re-examination and 21 (30%) were lost to follow-up.

B) Modification of study protocol and plan of work

The experience of the first 2 years of field activity indicated that a screening program by PE could not attain high coverage in this urban population. The positivity rate (2.4%) was sufficiently low to make this type of intervention cost-effective provided that the positive predictive value and sensitivity of the test proved to be high. At the end of 1998 the positive predictive value of the screening test appeared rather low but we had to wait until all incident cases were identified and linked to the cohort for a definitive measure. We planned to estimate sensitivity by comparing the incidence of interval cancers (not detected by screening) in the intervention group, with the incidence in the control group. Incident cases have been identified through the two population-based cancer registries serving Metro Manila. The results are given in section D) below.

Revision of study protocol.

In October 1997 we submitted a revision of the study protocol which was accepted by the US Army Medical Research Command. The revision of the study entailed discontinuing the intervention after completion of the first round and undertaking of follow up of the target population. The scope of the follow-up was to provide information on the effectiveness of the prevalent screen (incidence and mortality rates in the two groups). We proposed to follow up the two cohorts (intervention and control) for 10 years to study the onset of breast cancer and resulting mortality in relation to screening. We also planned to evaluate the association between reproductive factors and cancer of the breast in the intervention cohort. No comprehensive analytical study has ever been conducted to explain the relatively high incidence of breast cancer in this population still characterized by fertility rates typical of

developing countries but showing patterns of cancer risk quite high for Asian standards. Details on this proposal were given in the protocol revision and in previous annual reports.

We have now completed the follow up of the cohorts in the first 2 years. The results, described in section D), provide a basis for a new proposal described in section E).

C) Follow-up phase.

The follow-up of the intervention and control cohorts consisted in identifying women who developed breast and other cancers, those who died from other causes and those who migrated outside the study area. For this purpose a database of all death certificates occurring in the resident female population have been created and updated regularly until December 2001 together with the files of the cancer registries.

Years 1998 and 1999 were devoted to the completion of databases from the intervention phase, clinical follow-up and management of women positive for a lump and the development of follow-up procedures. In year 2000 we completed the collection of interview data on the prevalence of risk factors for breast cancer in women resident in the control areas. In the same year, the project entered the phase of routine follow up that continued throughout the end of 2001. During 2001 the identification of incident cases in years 1995-1998 was completed.

C.1 Procedures.

Procedures to computerize the data collected on incident cases and death certificates have been established and regular data entry ensures the maintenance of these databases. Data entered are subject to systematic checks for errors of coding and typing and for inconsistencies in the information recorded.

Follow-up procedures to match the master file and lists of the eligible populations (intervention and control cohorts) with the files of newly diagnosed cases and death certificates have been developed and tested. This takes advantage of a software program developed in Lyons for the purpose of identifying records pertaining to the same woman. The program makes use of the usual basic demographic items - names and surname, date of birth, age and detailed address - and allows for differences in spelling, or variations in the reported date of birth. Each variable contributing to the matching process is assigned a weight, which summarizes its discriminating power and the likelihood that it is reported incorrectly. Weights are added up to give a resulting matching score. Records matched are distinguished in three groups depending on the value of the matching score: 1) records definitely matching; 2) records that need manual verification; 3) records of different women. Records in group 2) are verified on paper documents and a decision is made.

D) October 2001 - September 2002 achievements.

Three have been the main activities in the period reported:

1. Case identification. Record linkage was performed between the cohort files and the files of the eligible population as identified in 1997, with the files of the breast cancer registry.
2. Nested case-control study. A case-control study, based on the cases identified by record linkage, nested in the intervention cohort was designed and completed.
3. Data analyses, still on-going.

D1. Death certificates.

We have assessed the inability to obtain information on all deaths occurring among resident women. Project staff All-causes periodically abstracted information from death certificates at the vital statistics offices of the 12 municipalities. However, access was discontinuous and substantial omissions were evident. Moreover, the distribution of causes of death among records encoded in the first 6 months showed significant biases with cancer being over-represented. The collection of this information was therefore abandoned.

D2. Record linkage between Master Files (MFs) of women interviewed and lists of the eligible population.

Lists of the eligible population for the intervention and control areas were derived from electoral rolls. Unfortunately these did not make provision for full address and only age instead of date of birth was available for residents of many administrative districts. The information that could be utilized for record linkage was therefore very limited giving rise to many dubious and unsolvable matches when record linkage was performed between these lists and the MFs of women interviewed. We adopted a conservative attitude maintaining only matches that scored 100%. As a result only a trivial proportion (<3% depending on the municipality) of the women interviewed and examined in the intervention were linked with records of women in the electoral rolls.

D3. Identification of incident cases.

The file of incident breast cancer cases in years 1995-1999 have been linked with intervention and control cohorts (population lists), with the screen cohort (master files) and with the files of women positive at PE. The results are given in figure 1. Two-hundred and eighteen and 211 new cases were identified among women in the electoral rolls of control and intervention arms respectively. The cases identified among screened women were 132 of which 81 among screen-negative. Of the 51 cases that occurred among screen-positive women only 31 were diagnosed through the intervention (table 4). The sensitivity of the program in detecting breast cancer was very low 23.5%, the positive predictive value was 0.9%. These measures are rather conservative since we assumed that all the cases detected in the first 2 years of follow-up were screen-detectable at time of intervention. Assuming that only cases in the first year of follow-up were false negative, sensitivity increases only by about 2% (25.7%) and the positive predictive value decreases to 0.8% of screen-positives.

D4. Active follow-up and re-interview of the 1,101 women of the case-control study nested in the screened cohort.

In years 2000-2001 we designed a case-control study nested in the cohort of screened women. The objectives of this study were 1) to assess how stable is the study population in view of a long-term follow-up and 2) assess the reliability of the interviews collected at time of examination.

At that stage we had identified 123 cases in the screened cohort. Eight controls were randomly selected from among all women in the cohort having the same age (± 2 years), date of interview and PE (± 4 months) and municipality of residence. A preliminary analysis of the risk of breast cancer associated with reproductive factors based on information collected at first examination was presented in the previous report (table 6). We observed a strong association with parity: the incidence of breast cancer was 3 times greater in women with no children compared with women with 6 or more full-time pregnancies (OR=3.3, 95%cl 1.6-6.7). Their risk was even greater when compared with women who had their first child before age 19 (OR=4.8, 95%cl 1.8-13.2). We also observed clear dose-response relationships with increasing parity and age at first child.

During the last year of activity the 1,101 women included in the nested case-control study were searched at original address and, if traced, interviewed my means of the same questionnaire used at time of intervention. The outcome of the follow-up is given in figure 4. Twenty percent of the controls had moved away or had died (2% of all controls). Four-hundred and seventy-eight were located at original address, of these 359 (37% of all) complied with re-interview. Among the cases 30 had moved away (24%), 52 had died (42%), 34 (28%) were located, of these 27 (22% of all) complied with interview.

These data show that long-term follow-up of the whole screened cohort is not feasible. However, the sub-cohort of women still present at original address 2 years after may represent a stable population suitable for further analytical studies.

The analyses of all data accumulated are ongoing. We plan to submit a revision of the plan of work justified by the results obtained thus far.

(6) KEY RESEARCH ACCOMPLISHMENTS

- Impact of the intervention by PE on mortality from breast cancer.
- Risk of cancer of breast in relation to several characteristics of women's reproductive life, obesity, height, alcohol consumption, family history of breast cancer and tobacco smoking.
- Prevalence of risk factors for breast cancer in the female population of Metro Manila.
- The same factors above plus education and socio-economical level as determinants of stage at diagnosis of breast cancer and survival, taking account of treatment received.
- Determinants of compliance with early diagnosis and treatment in a developing country.

(7) REPORTABLE OUTCOMES

- Poster presentation at the Era of Hope Conference, Washington D.C., 1-4 October 1997.
- Poster presentation at the Era of Hope Conference, Atlanta, 8-11 June 2000.
- Poster presentation at the second Era of Hope Department of Defense Breast Cancer Program Meeting, Orlando, Florida, 25-28 September 2002.
- REC-LINK software program – for automatic matching of records based on personal id-items (e.g. name, surname, age, date of birth, address).
- Data base of the female population resident in Metro Manila in years 1995-1996.
- Data base of new cancer cases diagnosed in the resident population 1990-1999.
- Data base of incident breast cancer cases, years 1995-1999, with clinical details of stage at diagnosis and initial treatment.

(8) CONCLUSIONS

The program as a whole is not expected to reduce mortality from breast cancer in this population due to the low compliance with clinical investigation and treatment of women found positive at PE. All remedies put in place to overcome, at least, logistical problems linked to referral failed to improve the compliance.

None of the cases detected through the intervention had distant metastasis, while 19% of the screen-positive who refused further investigation and 20% of the screen-negative were advanced at diagnosis.

During the first year of follow-up, the cancer registries have identified breast cancer cases presenting with advanced disease, who were positive at PE and refused further investigation one-two years earlier. This suggests that a small breast lump, which does not cause distress, is not perceived as something threatening one's health; it is only when the disease affects other organs that the woman seeks medical attention. This indicates that priority should be given to information and education of the population on the potential benefit of early detection. A better understanding of the cultural determinants of the attitude of this population towards health practices would help the Department of Health in developing future strategies.

The association between reproductive factors and cancer of the breast has never been studied in a prospective study of this size in a population with fertility rates characteristic of developing countries but showing incidence rates quite high for Asian standards. We will evaluate in detail the proportion of cases that is attributable to classic risk factors linked to reproductive variables. A crude estimate based on the results given in table 6 is that less than one third of all cases is attributable to low parity (0-2 children) or delayed first pregnancy (at age 21 years or later).

We will evaluate the feasibility of a study of genetic determinants of the risk of breast cancer in this population, based on the reported family history. The objective would be to assess if Philippino women are more susceptible to breast cancer than other ethnic groups.

Table 1. Description and size of the databases completed as a result of the intervention and of those maintained for the follow-up of the cohorts.

Intervention:

File	Content	No. of records
Master file	Nominal list of all women interviewed and offered PE. Includes 10% who refused PE	153,869
Referrals	Nominal list of all women detected positive at 1st PE by nurses. This file contains also the details of clinical follow up and final diagnosis.	3,490
Intervention population lists	Lists of the eligible population resident in the intervention HCs in the years when the intervention was conducted.	218,928
Control population lists	Lists of the eligible population resident in the control HCs in the years when the intervention was conducted.	191,086
Repeated exams	Outcome of two examinations performed a year apart in a subgroup of the intervention cohort.	3,000
Control interviews	Interviews of a sample of 1,000 women resident in control HCs.	999

Follow-up, performed by the two cancer registries:

Breast cancer cases	Detailed information on diagnoses (date, base and morphology if available), stage and survival of all new breast cancer cases diagnosed in Metro Manila.	3,300
Death Certificates	File of all deaths occurring in the resident population (women, age 30+), all causes. Only records encoded.	6,000
All cancer cases	Basic information on diagnosis and survival of all malignant cancer cases diagnosed in the resident population. Females.	years 1995-1999 7,000
Incident cases in the intervention and control populations	Breast cancer cases diagnosed among the women who were examined in the intervention areas or in the cohort of women.	169
Nested case-control study	• 123 cases identified in the intervention cohort in the first 2 years of follow-up, and 923 controls matched from the same cohort. • Active individual follow-up of all these women and re-interview of those traced.	1,101
Breast cancer incident cases identified in the pool of project files	Breast cancer cases linked with records in any of the following: intervention cohort, control cohort, population lists of intervention and control areas.	523

Table 2.
Results of the single round screening, completed in December 1997.

Intervention		
No. interviewed	153,869	
No. interviewed and examined	147,558	
Compliance		96%
Women detected positive		
Number of women detected positive and referred to tumor clinics	3,490	
positivity rate:		2.4%
No. referred who completed the diagnostic process:	1,108	
percent compliance (includes women visited at home):		31.8%
of which, No. referred who did not attend clinic and were visited at home	631	
No. with final diagnosis among women visited at home:	585	93.7%
Outcome of diagnoses (3,492 women):		
no mass	545	15.6%
malignant breast cancer:	31	0.9%
benign breast disease:	532	15.2%
actively refused further investigation (at clinics or home visits):	1,476	42.3%
attended other clinic:	73	2.1%
pending diagnoses:	71	2.0%
not traced at initial address or died:	762	21.8%

Table 3.
Comparison of characteristics of women who refused examination and those who accepted.

	compliers N=92,091	refusers N=12,404	control sample N=999
age in years (mean±SD)	44.9±8.3	44.9±8.6	46.6±8.0
mean age at menarche	13.7±1.7	13.6±1.6	13.0±1.4
mean age at first fullterm pregnancy	23.2±4.6	23.9±4.9	21.6±3.8
ever used contraception (%)	33.0%	26.9%	19.8%
nulliparous (%)	9.7%	15.7%	4%
never had a PAP smear (%)	70.6%	71.0%	74.9%
smokers (%)	8.2%	7.5%	5.0%
drinkers (%)	7.7%	12.5%	26.3%

Table 4_ Follow-up.
Breast cancer cases identified among 3,490 screen-positive women, by outcome at time of intervention.

Outcome at time of intervention	BC	screen-positive
Screen-positive (total 51):		
malignant cancer	31	31
benign disease	4	1,148
lost to follow-up, moved or died from other cause	9	762
refused biopsy	6	1,476
Referred to other hospital	1	73
Screen-negative	81	147,558
	51	3,490
Positive predictive value =	0.9%	
Program sensitivity %= 31/132	23.5%	

Table 5 Follow-up
Breast cancer cases that occurred among screened women. Distribution by stage and screening outcome.

	Unknown	Loc.	Reg.	Dist	*In situ*	Total
Breast ca. detected by the intervention	14	**2**	**15**	**0**	**0**	31
% of stage determined		11.8	88.2	0.0	0.0	
Screen-positive lost to follow-up or clinical diagnosis of benign disease	4	**2**	**11**	**3**	0	20
% of stage determined		12.5	68.8	18.8	0.0	
Screen-negative	15	**12**	**40**	**13**	**1**	81
% of stage determined		18.2	60.6	19.7	1.5	
Total	33	**16**	**66**	**16**	**1**	132
% of stage determined		16.2	66.7	16.2	1.0	

Table 6. Numbers of cases and controls, odds ratios (RR) and 95% confidence limits by levels of risk factors. OR estimates by unconditional logistic regression.

Factor	No. cases	No. controls	OR	95% c.l.
Family income (*):				
<667 §	25	223	1.	
667-	26	185	1.3	0.7-2.3
1167-	22	190	1.0	0.6-2.0
1875+	28	205	1.2	0.6-2.4
Unknwon	22	176	1.1	0.6-2.1
Age at menarche (years):				
<12	11	71	1.3	0.6-2.8
12-	27	182	1.3	0.7-2.2
13-	52	438	1.0	0.6-1.7
15+ §	32	276	1.	
Unknwon	1	11	0.8	0.1-6.3
No. of full-term pregnancies:				
Nulliparous	25	115	3.3	1.6-6.7
1-2	30	161	2.7	1.4-5.4
3	16	161	1.4	0.7-3.1
4-5	23	244	1.3	0.6-2.6
6+ §	14	193	1.	
unknown	15	104	2.2	0.9-5.0
Age at first pregnancy (years):				
<19 §	79	420	1.	
19-21	5	105	1.5	0.5-4.5
21-24	10	141	2.1	0.8-5.7
25+	22	220	3.7	1.5-9.6
nulliparous	25	115	4.8	1.8-13.2
unknown	7	92	0.9	0.2-3.9
Age at menopause (years):				
<45§	6	64	1.	
45-47	12	65	2.0	0.7-5.6
48-50	5	61	1.0	0.3-3.4
50+	18	97	2.3	0.8-6.3
Premenopausal & unknown	82	691	1.1	0.5-2.8

(*) Average annual income per family cohabitant in Pesos.
§ Reference category for the OR.
OR adjusted for age and residential area.

Figure 1.

Follow-up to 1999 – New cases of breast cancer identified in control (218) and intervention (211) arms as defined by electoral rolls. New cases in the intervention cohort (132) of which 48 were also linked with records in the lists of the population.

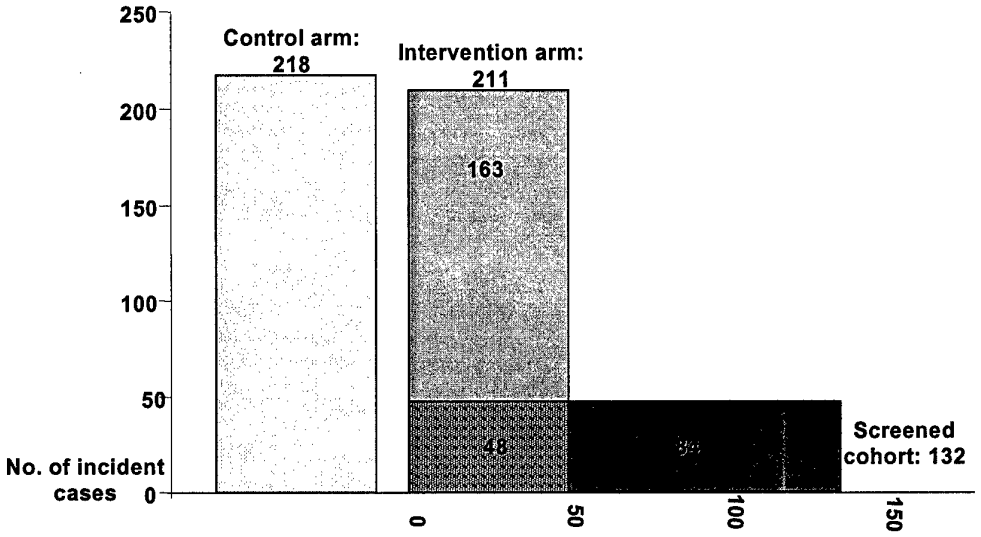


Figure 2.

Follow-up to 1999 – New cases of breast cancer identified in the screened cohort by screening outcome. Total 132 cases.

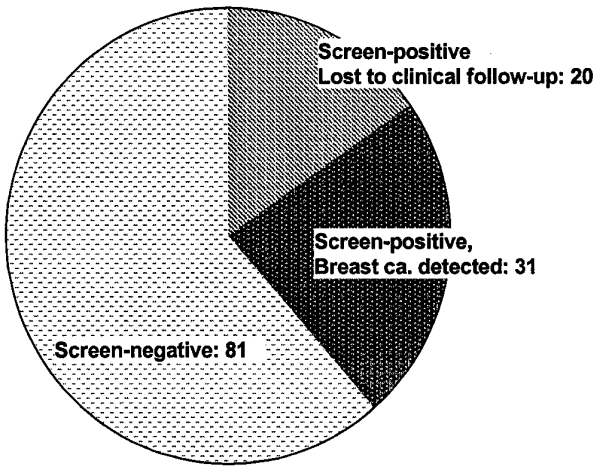


Figure 3.
Incident cases by stage in the two arms defined by electoral rolls.
Percent and 95% c.l. of 211 and 218 cases in intervention and control arm respectively.

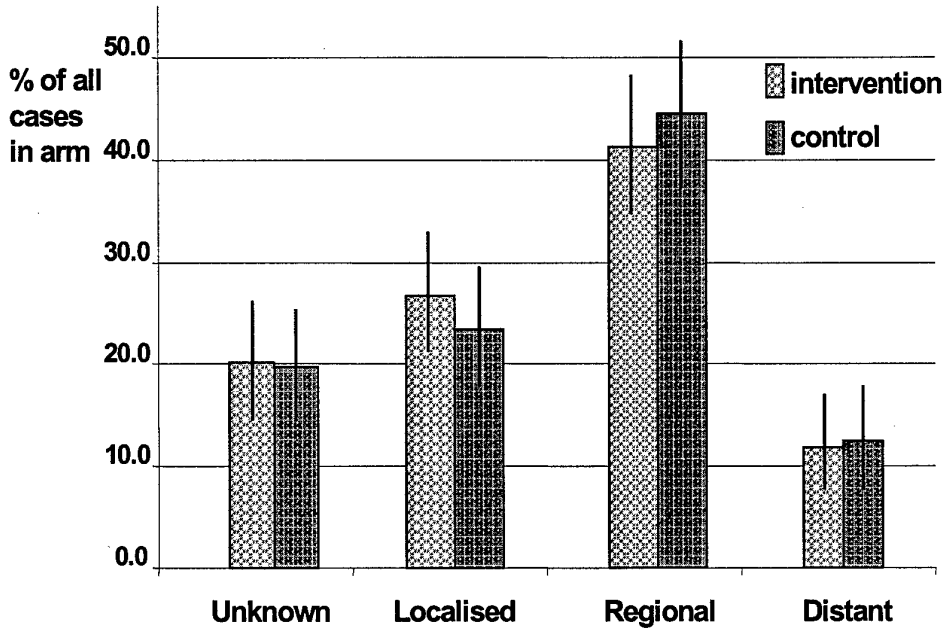
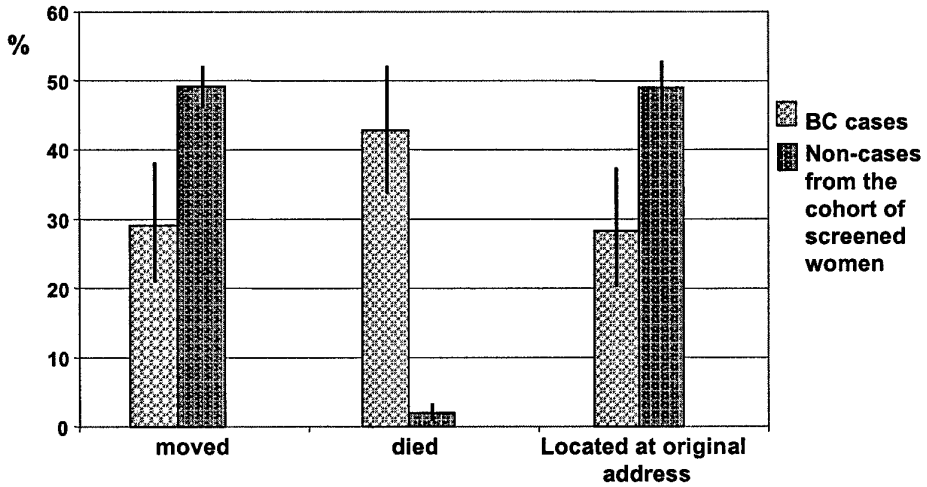


Figure 4.
Nested case-control study. Outcome of individual follow-up of 123 cases and 978 matched controls. Relative frequencies and 95% c.l.



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